

## Revisiting the term *neuroprotection* in chronic and degenerative diseases

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### Abstract

Thanks to the development of several new researches, the lifetime presented a significant increase, even so, we still have many obstacles to overcome – among them, manage and get responses regarding neurodegenerative diseases. Where we are in the understanding of neuroprotection? Do we really have protective therapies for diseases considered degeneratives such as amyotrophic lateral sclerosis and its variants, Parkinson's disease, Alzheimer's disease and many others? Neuroprotection is defined by many researches as interactions and interventions that can slow down or even inhibit the progression of neuronal degeneration process. We make some considerations on this *neuroprotective effect*.

### Some considerations

Time is relentless and cruel, although it is often helpful to understand live. Search for strategies to avoid the wear it produces in our

brain machinery, is undoubtedly distressing; considering that every second corresponds to a second that does not return. In the early history of humankind the average life was reduced due to its fragility in the face of diseases and especially of the strongest predators. With the development of research in Medicine, lifetime presented a significant increase; yet we still have many hurdles to overcome – among them manage and get responses regarding neurodegenerative diseases. With aging we lost cells, the cell division mechanism becomes slowed, DNA mutations tend to occur (disorienting the cell command), the energy supply by mitochondrial damage is affected, etc. Cytoplasmic inclusions and protein aggregates form a non-degradable brain trash, and relationship with environmental factors is still unclear, among other factors.<sup>1,2</sup> Fortunately medicine is improving every day and it tries to respond to such mechanisms.

We assume to treat that term alone, as well as the criticism of our colleagues. It is insane to talk in neuroprotection without mentioning pathophysiology. In fact, what do we mean by neuroprotection? Do we really have protective therapies for example, for diseases such as amyotrophic lateral sclerosis (ALS) and its variants, Parkinson's disease, Alzheimer's disease and cerebellar ataxias? Many authors define neuroprotection as interactions and interventions that can slow down or even inhibit the progression of neuronal degeneration.<sup>3</sup> In this context it scares us our small/primate knowledge about the pathophysiological framework of these diseases. The pathophysiology is broad and interconnected. It takes us to a puzzle with pieces that do not end, either fit together and seems to be lacking. When the model appears to be fitting together, a new breakthrough appears and everything is undone. So far, neuroprotective therapies for neurodegenerative diseases are just theoretical, awaiting further researches, mainly through gene mapping. We are sure that after this provocative communication thousands of criticism will be raging like wildfire. This is the science. Even in the double blind studies, controlled and randomized, that *try to* fit patients at the same stage of disease with all caution, introducing new drugs and monitor the natural history of the disease by well-defined periods and instruments, there is a flaw – the individuality of the human being. Why do some patients in our clinic have survival of 20 or more years of clinical and electrophysiological diagnosis of ALS? Why do individuals with progressive spinal amyotrophy, sporadic adult form, have an overwhelming presentation of the disease that causes death in months? There are certainly new *neuroprotective* mechanisms, obscure and built into each one of us.<sup>4,5</sup> Stephen William Hawking, for example, when received the diagnosis of

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ALS, was advised not to hold his time with a book he was writing because he had no lifetime. The physicist not only finished that book, as he married and had children. We are currently following a young man aged 25 with a diagnosis of progressive spinal amyotrophy three years after clinical onset.

The reader will probably wonder - how to do something different then? Today, unfortunately, it is what fills us and what we have to contribute, as the human being does not come with an instruction manual, especially when many of his brain parts are already battered and are irreplaceable. These diseases are big *icebergs*: when the damage hatch in neuronal network is at least scary. Before that, our central nervous system has already tried quietly and certainly in every way to repair our system.

Neurodegenerative diseases represent one of the great challenges of the current neuroscience. Parkinson's disease, for example, affects millions of individuals worldwide, and the number of patients is expected to double over the next 20 years. It is therefore natural that Parkinson's disease is the object of intense research in order to understand its etiology and develop possible treatment strategies.<sup>6,7</sup> It has been recently identified that in Parkinson's disease when motor manifestations occur, about 60-80% of substantia nigra neurons have already succumbed to the disease process. Many authors even wonder if the idiopathic Parkinson's disease really exists or in fact, they are similar phenotypes to stories of different evolution.

In Alzheimer's disease and other forms of irreversible dementia, aging is part of a multifactorial process. Many studies have pointed to

autophagy for neuroprotective strategies in aging and in neurodegenerative diseases such as this, with a focus on sub-cellular changes related to cell death.<sup>8</sup>

Anyway, we will continue fighting to alleviate the suffering of our species, with dedication, competence and especially medical and scientific commitment. The evidence-based medicine helped us a lot, however there is always someone who does not fit this context. The individuality of diseases process continues to be a challenge for *neuroprotection*.

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